In the matter of US
Patent Application
Serial No. 725206
filed April 19th, 1985

#16

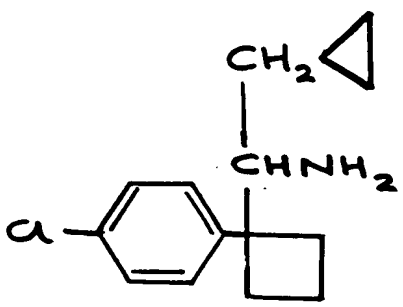
Declaration

I, Gerrard Haran, a British subject of 57 Zulla Road, Mapperley Park, Nottingham, England do hereby declare that:-

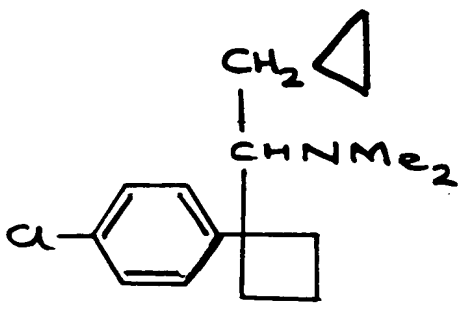
1) In 1969, I attained a B.Sc Hons. (Chemistry), from Glasgow University (Scotland) and in 1972, I completed a period of research in inorganic chemistry at Glasgow University (Scotland) which led to the award of a degree of Doctor of Philosophy.

2) I joined The Boots Company as a Research Chemist responsible for infra-red and nuclear magnetic resonance spectroscopy in 1974. In 1980, I was promoted to the post of Section Head of Physical Chemistry with the additional responsibility of gas chromotography. In this position I advise my colleagues within The Boots Company on the interpretation of nuclear magnetic resonance spectra.

3) In October 1984, at the request of Dr. J.E. Jeffery, staff under my direct control, using standard procedures, obtained proton nuclear magnetic resonance spectra of two compounds which were described in the above identified patent application as Examples 10(u) and 11(g) respectively. Structures I and II below had been assigned to these compounds at the time of their preparation in 1981. The compounds were in the form of hydrochoride salts.



I

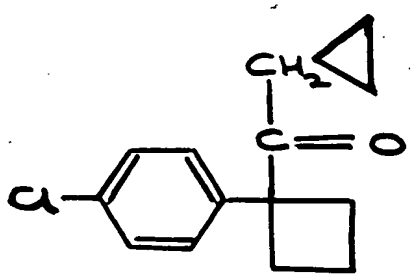


II

The spectra obtained are attached hereto as Figures I and II.

4) I have examined these spectra and consider that signals at 6.00 δ to 5.48 δ which represent one proton and at 5.24 δ to 4.92 δ which represent two protons in the spectrum reproduced in Figure I and the signals at 6.10 δ to 5.54 δ which represent one proton and at 5.32 δ to 5.00 δ which represent two protons in the spectrum reproduced in Figure II show the presence in these two compounds of a $-CH=CH_2$ group. There are no signals at 0-1 δ which would indicate the presence of a cyclopropyl ring as shown in structures I and II. I therefore concluded that Structures I and II assigned to these compounds were incorrect.

5) In February 1986, at the request of Dr. J.E. Jeffery, staff under my direct control, using standard procedures, obtained a proton nuclear magnetic resonance spectrum (attached hereto as Figure III) of a ketone to which Structure III had been assigned at the time of its preparation in 1981.



III

The signals at 5.96 δ to 5.40 δ representing one proton and at 5.10 δ to 4.72 δ representing two protons show the presence of a $-CH=CH_2$ group. There are no signals at 0-1 δ which would indicate the presence of a cyclopropyl ring as shown in structure III. I therefore concluded that Structure III assigned to this ketone was incorrect.

Further declarant sayeth not

I, the undersigned declare further that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that wilful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States code and that such wilful false statements may jeopardise the validity of the application or any patent issuing thereon.

Gerrard Haran

Gerrard Haran
Signed at Nottingham, England on the 24th day of March, 1987.

Figure I

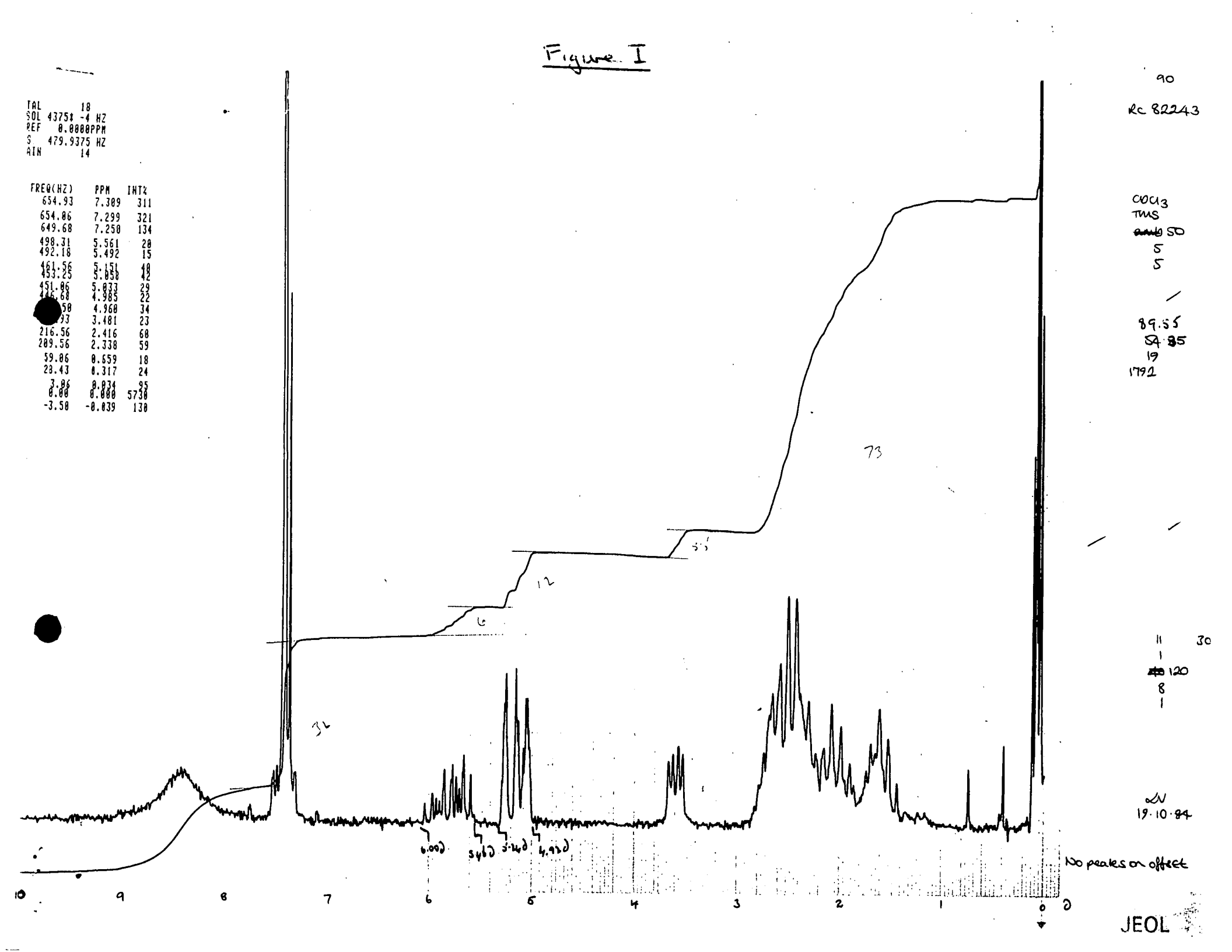
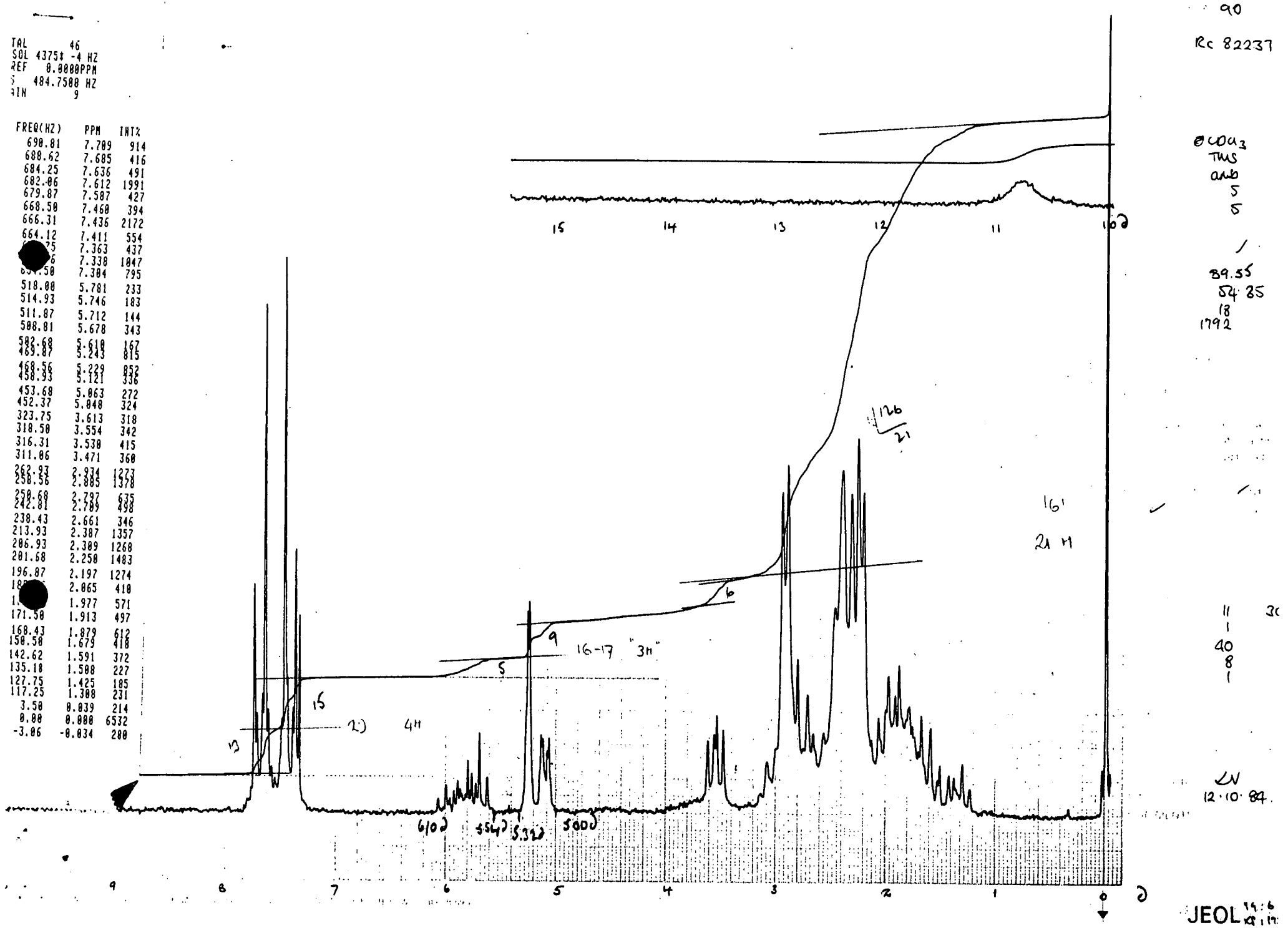

TAL 18
SOL 4375± -4 HZ
REF 0.0000PPM
S 479.9375 HZ
AIN 14
FREQ(HZ) PPM INT%
654.93 7.309 311
654.06 7.299 321
649.68 7.250 134
498.31 5.561 20
492.18 5.492 15
461.56 5.151 40
453.25 5.058 42
451.06 5.033 29
446.68 4.985 22
444.50 4.960 34
311.93 3.481 23
216.56 2.416 60
209.56 2.338 59
59.06 0.659 18
28.43 0.317 24
3.06 0.034 95
0.00 0.000 5730
-3.50 -0.039 130
90
Rc 82243
CDCl3
TMS
50
5
5
89.55
85
19
1791
11
1
120
8
1
30
19·10·84
100 peaks on offset
6.00d
5.46d
5.24d
4.92d
73
32
12
6
5.1
10
9
8
7
6
5
4
3
2
1
0
JEOL

Figure II



90

Rc 82237

$CDCl_3$
TMS
amb
5
5

89.55
54.85
18
1792

1126
21

16'

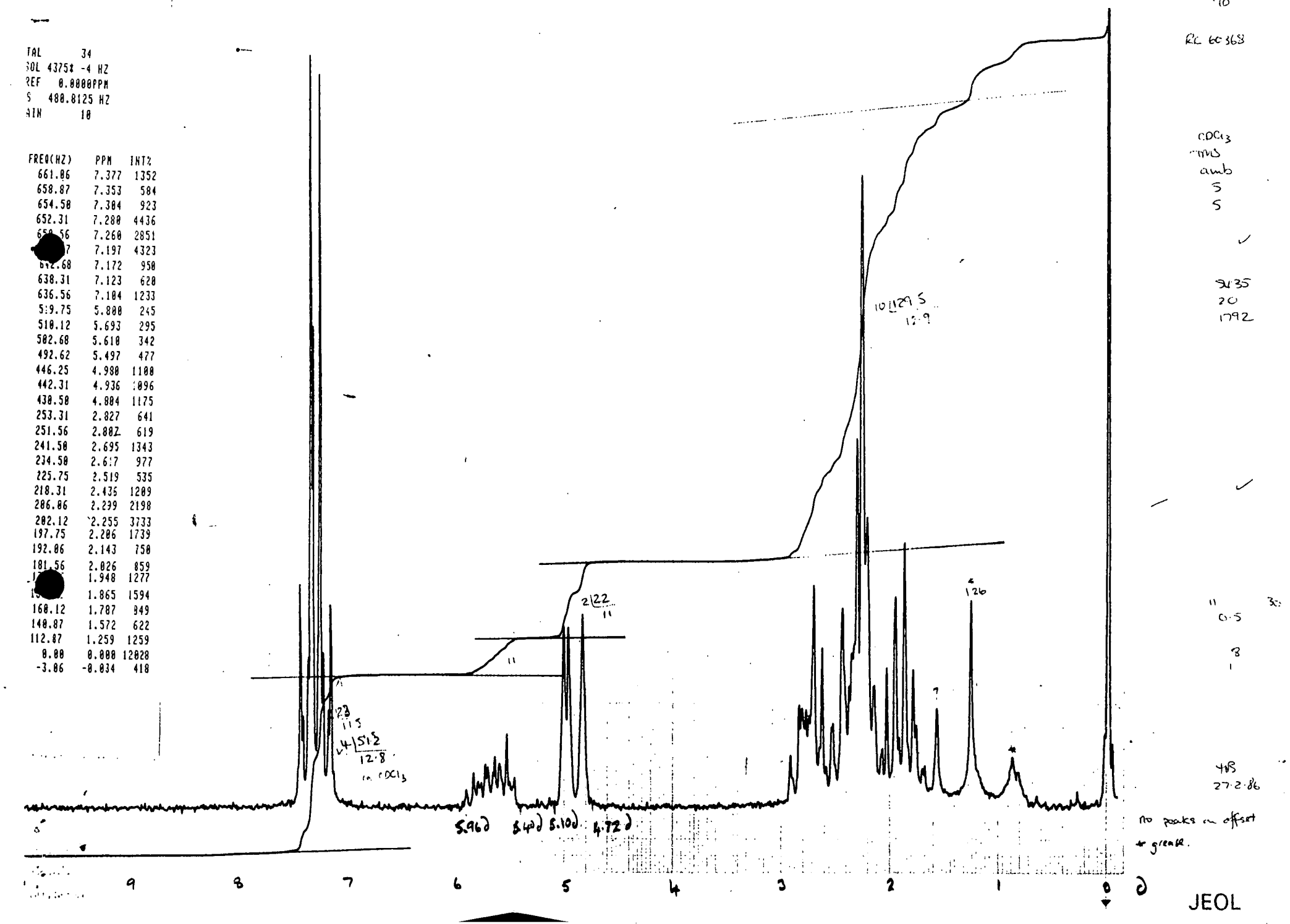
21 H

11
1
40
8
1

12·10·84.

JEOL

Figure III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SOL 4375% -4 HZ
REF 0.0000PPM
S 488.8125 HZ
AIN 10
FREQ(HZ) PPM INT%
661.86 7.377 1352
658.87 7.353 584
654.50 7.304 923
652.31 7.280 4436
650.56 7.260 2851
647 7.197 4323
642.68 7.172 950
638.31 7.123 620
636.56 7.104 1233
519.75 5.800 245
510.12 5.693 295
502.68 5.610 342
492.62 5.497 477
446.25 4.980 1100
442.31 4.936 1096
438.50 4.894 1175
253.31 2.827 641
251.56 2.807 619
241.50 2.695 1343
234.50 2.617 977
225.75 2.519 535
218.31 2.436 1209
206.86 2.239 2198
202.12 2.255 3733
197.75 2.206 1739
192.06 2.143 758
181.56 2.026 859
1.948 1277
1.865 1594
168.12 1.787 949
140.87 1.572 622
112.87 1.259 1259
0.00 0.000 12028
-3.06 -0.034 418
5.96d
8.40d
5.10d
4.72d
JEOL